Performance evaluation of Meropenem-Vaborbactam on clinical isolates in a fully automated rapid AST system

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Background

In recent years, Meropenem-Vaborbactam (Mer-Vab) has become a valuable option for treating critically ill patients suffering from serious multidrug-resistant infections. Consequently, there is a need to test bacteria susceptibility against this β-lactam/β-lactamase inhibitor combination when guiding treatment[1–4].

ASTar® allows rapid Antimicrobial Susceptibility Testing (AST) directly from positive blood cultures[5]. ASTar performance when testing Mer-Vab was evaluated against ISO 20776-2:2007.

Fig 1. ASTar Instrument.

Materials and methods

ASTar data was generated for Mer-Vab at three sites in the US as well as one internal site. Data was compared to broth microdilution (BMD) performed according to CLSI M07, 11th edition[6].

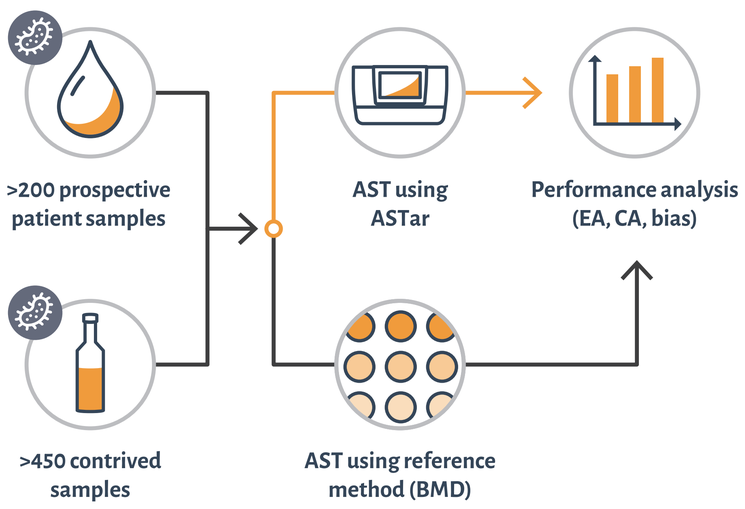

Fig 2. Over 200 prospective patient samples and more than 450 contrived samples containing different Enterobacterales species (*E. coli, K. pneumoniae, K. oxytoca, K. aerogenes, C. freundii, C. koseri, E. cloacae* complex, *M. morganii, P. mirabilis, P. vulgaris, S. marcescens*) were evaluated in the study. Bias was calculated following ISO 20776-2:2021.

References

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Conclusion

- The last resort β-lactam/β-lactamase inhibitor combination Meropenem-Vaborbactam has been successfully added to the broad antimicrobial panel on offer from ASTar.
- The performance evaluated for Meropenem-Vaborbactam was in accordance with ISO 20776:2-2007, and the measured bias was in alignment with the new standard ISO 20776:2-2021.
- The expansion of the ASTar BC G– Kit panel enables susceptibility results reported for Meropenem-Vaborbactam after approximately 6 hours from the start of testing. The same is true for all tested antimicrobials, making ASTar a useful tool to guide physicians in the treatment of bloodstream infections.

Results

MIC data was interpreted to category using EUCAST clinical breakpoints version 14.0[7], and EA and CA were assessed in accordance to ISO 20776-2:2007[8]. The measured Essential Agreement (EA) for Mer-Vab was 96.8%, Categorical Agreement (CA) was 99.6%, and reproducibility of 100%, fulfilling ISO performance requirements (Table 1 and 2).

Two major discrepancies and one very major discrepancy were recorded, the latter was within EA. The assessed isolate population was composed with the intent to include resistant isolates. The incidence of resistant isolates was low, which can be expected for a new drug whereby a single discrepancy leads to a very major discrepancy, VMD, that exceeds 3%.

Table 2. ASTar performance data and error rates for Meropenem-Vaborbactam.

Antimicrobial agent	ASTar vs. reference BMD			
	EA #/tot (%)	CA #/tot (%)	VMD	MD
Meropenem-Vaborbactam	673/695 (96.8%)	692/695 (99.6%)	1/7	2/688

In the most recent AST performance standard, ISO standard 20776:2-2021, bias is introduced to evaluate MIC data without the need of clinical breakpoints. Bias should fall within ±30%, calculated on at least 25 on-scale data points[9]. For Mer-Vab testing using ASTar, bias was within the acceptance criteria at –25.4% (Table 3).

ASTar bias for Meropenem-Vaborbactam is –25.4%

Table 1. ASTar performance data.

Antimicrobial agent	ASTar vs. reference BMD	
	EA #/tot (%)	CA #/tot (%)
Amikacin	413/448 (92.2%)	442/448 (98.7%)
Amoxicillin-Clavulanic acid	341/357 (95.5%)	332/357 (93.0%)
Ampicillin	233/241 (96.7%)	237/241 (98.34%)
Aztreonam	421/427 (98.6%)	421/427 (98.6%)
Cefazolin	276/286 (96.5%)	262/286 (91.6%)
Cefepime	440/452 (97.4%)	435/441 (98.6%)
Cefotaxime	422/443 (95.3%)	438/443 (98.9%)
Ceftazidime	389/400 (97.3%)	387/400 (96.8%)
Ceftazidime-Avibactam	393/429 (91.6%)	422/429 (98.4%)
Ceftazidime-Tazobactam	416/426 (97.7%)	418/426 (98.1%)
Ceftriaxone	429/444 (96.6%)	440/444 (99.1%)
Cefuroxime	282/294 (95.9%)	285/294 (96.9%)
Ciprofloxacin	431/447 (96.4%)	429/447 (96.0%)
Colistin	237/251 (94.4%)	251/251 (100%)
Ertapenem	391/413 (94.7%)	412/413 (99.8%)
Gentamicin	412/431 (95.6%)	423/431 (98.1%)
Levofloxacin	466/475 (98.1%)	459/475 (96.6%)
Meropenem	455/481 (94.6%)	461/481 (95.8%)
Meropenem-Vaborbactam	673/695 (96.8%)	692/695 (99.6%)
Piperacillin-Tazobactam	416/436 (95.4%)	426/436 (97.7%)
Tigecycline	189/196 (96.4%)	195/196 (99.5%)
Tobramycin	428/451 (94.9%)	448/451 (99.3%)
Trimethoprim-Sulfamethoxazole	403/423 (95.3%)	410/423 (96.9%)
Total	**8956/9346 (95.8%)**	**9125/9335 (97.8%)**

Table 3. Distribution of MIC results for ASTar compared to reference BMD. Green and grey boxes = within EA; green = on target. Red lines = clinical breakpoints.

ASTar MIC	Ref MIC ≤0.25	0.5	1	2	4	8	16	32	>32	Total
≤0.25	647	3	3							**653**
0.5	3									**3**
1	2	2		1		1				**6**
2	2	4	1	3		1				**11**
4		1	4	4	2					**11**
8				1	1		1			**3**
16						1	1	1		**3**
32						1			1	**2**
>32									3	**3**
Total	**654**	**10**	**8**	**9**	**3**	**4**	**2**	**1**	**4**	**695**

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